exposure scenarios. In comparing our rough "equivalent" estimates obtained based on lifetime exposure to concentrations currently being used for *in vitro* testing, we indeed intended to highlight that such concentrations represent a high end bounding limit, as Oberdörster has emphasized. Equivalent *in vitro* concentrations based on a 24-hr scenario are intended to represent more realistic short-term exposures.

We agree with Oberdörster that our article (Gangwal et al. 2011) should not be viewed as justification for using very high NM *in vitro* testing concentrations. Rather, we demonstrate the importance of understanding *in vitro* concentrations in the context of the potential for human NM exposure to improve study design and facilitate interpretation of testing results. For NMs currently being tested in the U.S. Environmental Protection Agency's (EPA) ToxCast project (Dix et al. 2007), we are in fact evaluating multiple concentrations based on consideration of potential exposure and generally have set NM testing concentrations to range from below the 24-hr inhalation exposure equivalent to the full working lifetime equivalent.

As we note in our article (Gangwal et al. 2011) and as Oberdörster has further emphasized, there are significant uncertainties associated with our estimates of exposure and associated dosing concentrations. These include uncertainties associated with screening-level tools available for modeling deposition of engineered nanomaterials and with our understanding of characteristics and properties of materials found in the human environment. In the interest of mining available tools to inform design of toxicity tests for immediate use, we did opt to make significant simplifying assumptions related to particle characteristics and to apply a version of the MPPD model adapted by the developers for application to nanofibers/nanotubes (National Institute for Occupational Safety and Health 2008). The modeled alveolar mass retained for CNTs based on more realistic, short 24-hr inhalation exposure duration is available online (U.S. EPA 2011).

One point that Oberdörster missed in our article (Gangwal et al. 2011) is that we calculated alveolar lung surface concentration using the same low estimate of human alveolar surface area for both the full working lifetime and the 24-hr exposure duration, and thus calculations for both exposure scenarios may be lower by approximately one order of magnitude.

We are pleased that our framework for using available exposure information to inform selection of *in vitro* toxicity testing concentrations is generating important discussion. We believe the issues and limitations raised in our article and by Oberdörster are important and demonstrate a critical need for continuing research to understand the potential for human exposure to engineered nanomaterials and to design environmentally relevant toxicity testing schemes.

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This response does not necessarily reflect official U.S. EPA policy.

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Bisphenol A in Thermal Paper Receipts: An Opportunity for Evidence-Based Prevention

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The recent report by Taylor et al. (2011) on the pharmacokinetics of bisphenol A (BPA) emphasizes the similarities between humans, monkeys, and mice in the metabolism of this ubiquitous and potentially toxic synthetic chemical. The authors suggested that human exposure to BPA may be "much higher than previously assumed." They observed that a potentially important nonfood source of exposure to BPA may be the thermal paper used in cash register receipts.

BPA is found in receipt paper (Mendum et al. 2010) and appears to transfer readily from receipts to skin (Biedermann et al. 2010) and to be absorbed transdermally (Zalko et al. 2011). Retail workers, who likely have more frequent exposure to cash receipts containing BPA than other Americans, have been found to have elevated levels of urinary BPA (Lunder et al. 2010). BPA has been shown to be capable of crossing the placenta (Balakrishnan et al. 2010) and to be toxic during early mammalian development (vom Saal and Hughes 2005). This toxicity is relevant to humans, given the similarities in BPA metabolism observed across species by Taylor et al. (2011). Prenatal exposure of human infants to BPA has been associated with behavioral anomalies (Braun et al. 2009).

There is a sense of déjà vu about this story: In the 1970s polychlorinated biphenyls (PCBs) were widely used in carbonless copy paper (Erickson and Kaley 2011). PCBs were shown to be absorbed through the skin (Carpenter 2006), and prenatal exposures to PCBs were subsequently shown to cause irreversible brain injury to developing fetuses, which resulted in permanent loss of IQ (intelligence quotient) and alterations in behavior (Jacobson and Jacobson 1997). This exposure ended when the manufacture of PCBs was banned in the United States in 1976.

The research of Taylor et al. (2011) contributes to our understanding of the potential harms to the developing fetus from BPA. These findings underscore the need to develop a new U.S. chemical policy that would require toxicological testing of widely used chemicals already on the market and premarket safety testing of all proposed new chemicals (Landrigan and Goldman 2011). The time to presume that chemicals are safe until they are proven beyond all doubt to cause injury to America's children is past. While research into the effects of exposure to BPA continues, we have an opportunity to act today on the basis of the available evidence to remove BPA from thermal paper, as we strive to protect the health and future intelligence of America's children.

The authors declare they have no actual or potential competing financial interests.

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Bisphenol A in Thermal Paper Receipts: Taylor et al. Respond

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We agree with Schwartz and Landrigan that there is a need for change in the regulatory system for chemicals used in products in the United States. Bisphenol A (BPA) is one of thousands of chemicals of concern, but it provides a striking example of what happens when there is no requirement for premarket testing. Full estrogenic activity was demonstrated for BPA when it was tested for use as a pharmaceutical drug in 1936, which should have precluded its use in the wide range of products that results in continuous exposure (Stahlhut et al. 2009). The findings we reported in our article (Taylor et al. 2011) show that clearance of BPA in mice, monkeys, and humans does not differ, and years of research has demonstrated that mice and rats are valid models for predicting the long-term adverse consequences of developmental exposure to estrogenic chemicals. A vast and rapidly growing number of studies with experimental animals (Richter et al. 2007) and humans (Braun and Hauser 2011) report adverse effects later in life as a result of exposure to BPA during development.

In the 2003–2004 National Health and Nutrition Examination Survey (NHANES) study, the Centers for Disease Control and Prevention estimated that 93% of people in the United States are exposed to BPA, with higher exposures in children than adults. The potential exposure of fetuses and infants to BPA is especially concerning because BPA is not metabolized effectively during these highly sensitive stages of human development. Our data (Taylor et al. 2011) indicate that to reach the median serum levels of unconjugated (bioactive) BPA reported in multiple biomonitoring studies (Vandenberg et al. 2010), exposure must be far higher than predicted by the Food and Drug Administration (FDA) based on its risk assessment of BPA (FDA 2008); these government estimates (FDA 2008) are based on kinetics after acute oral exposure and the assumption that food and beverage packaging is the only source of BPA exposure. However, data from the 2003–2004 NHANES (Stahlhut et al. 2009) confirmed that BPA exposure is likely to be from multiple sources—including thermal receipt paper—and there is evidence that in adults different forms of exposure do not have the same metabolic profile (Sieli et al. 2011).

We find it disturbing that government agencies continue to argue that the public should not be concerned about BPA because daily exposures are below "safe" levels. This conclusion is based on flawed studies using outdated approaches. We agree with Schwartz and Landrigan that we have to stop repeating the same mistakes made previously with chemicals such as lead, for which, after decades of repeatedly lowering "safe" exposure estimates, the current predicted "safe" level is still above levels now known to cause adverse effects. For endocrine-disrupting chemicals there are no threshold doses below which exposures are safe (Sheehan 2006), a reality that regulators are unwilling to acknowledge.

F.S.vS. consulted for an attorney involved in civil litigation regarding the health effects of BPA, but he has no financial interests related to plastics, products, or compounds that might serve as alternatives to BPA. The remaining authors declare they have no actual or potential competing financial interests.

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Artificial Food Color Additives and Child Behavior

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In his commentary, Weiss (2012) discusses results of the recent Food and Drug Administration (FDA) evaluation of the possible association between artificial food color additives (AFCs) and adverse behaviors in children, including those related to hyperactivity. The stated aim of the commentary is "to examine the basis of the FDA's position, the elements of the review that led to its decision and that of the committee, and the reasons why this is an environmental issue." In the commentary, however, *a*) the FDA's petition review and safety assessment processes are misconstrued; *b*) the range of normal behaviors and the levels at which these behaviors can be considered adverse are not distinguished, and comparisons that cloud the distinction are unsupported; *c*) examples from individual studies are used out of context or irrespective of the conclusions expressed by the authors; *d*) specific results are cited from studies the FDA concluded were fundamentally flawed; and *e*) comprehensive reviews by other scientific panels are not mentioned. As a result, the viewpoint presented does not properly characterize the public health issue, the FDA's evaluation and conclusions, or the processes involved, including the FDA's proposed actions. This letter addresses as many general errors, omissions, and apparent flaws in the commentary as space permits.

In 2008, the Center for Science in the Public Interest (CSPI) petitioned the FDA to ban eight AFCs based primarily on results from clinical challenge studies on behavioral effects of these chemicals in children with a history of hyperactivity disorders or related behavioral problems (CSPI 2008). The petition also cited studies that tested potential